Aim: To develop a model allowing an individualized prediction of the risk of liver-related death among patients with alcoholic cirrhosis, that takes into account the impact of abstinence.
Methods: Data related to death and causes of death were collected among patients with alcoholic cirrhosis consecutively seen in a single center during a 21-year period. Abstinence was defined as discontinuation of any alcohol intake within the first 12 months following inclusion. Multivariate Fine and Gray proportional hazards models were used to identify factors associated with liver-related death. We calculated Akaike information criterion values by adding variables using a forward step by step approach to build the best competing risk regression (CRR) model that predicts liver-related death. To validate the prediction of the model, a cross validation procedure was applied using a training set of 80% and a testing set of 20% of the data randomly chosen. The Brier score was used to estimate the quality of the prediction of the different models tested, the model with the lowest Brier score providing the best prediction.
Results: 489 patients (68% of male, median age 55 years [95% CI: 54-56], 45% Child-Pugh stages B or C, median MELD score 9.0 [95% CI: 8.5-9.7]) were included. During follow-up (median, 57 months), 247 patients died, 12 from hepatocellular carcinoma, 156 from liver failure and 76 from non-liver related causes. Three variables were independently associated with liver-related mortality: age (HR: 1.02, 95% CI: 1.01-1.04, p=0.01), Child-Pugh score (HR: 1.20, 95% CI: 1.11-1.29, p<0.001) and abstinence (HR: 0.42, 95% CI: 0.28-0.63, p<0.001). A CRR model using these 3 variables as covariates was built, providing a continuum risk of death at 5 years in abstainers and consumers. For any combination of age and Child-Pugh score, patients who did not abstain from alcohol had a greater risk of dying at 5 years than patients who abstained from alcohol. According to the Brier score, the prediction of liver-related death at 5 years was better using the CRR model than with the random model in 100% of the cases, with the Kaplan Meier model in 93%, and with the Cox model in 92%. The prediction of liver-related death was not better when the MELD score was used in the CRR model instead of the Child-Pugh score.
Conclusions: The CRR model combining age, Child-Pugh score and abstinence accurately predicts the risk of liver-related death on an individual basis among patients with alcoholic cirrhosis. Huge differences in 5-years prediction of death were observed in patients who abstained and who did not abstain from alcohol. This model may serve as a tool for prognosis assessment in a daily practice and may help to motivate patients to stop drinking.

A10

Is it too early to expand beyond the Milan Criteria for liver transplantation? A retrospective, multicentric study in Belgium.

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Introduction: Recent studies suggest that a subgroup of patients with liver cirrhosis receiving a liver transplantation (LT) for hepatocellular carcinoma (HCC) beyond the Milan Criteria (MC) can achieve a similar overall and tumor-free survival. Consequently alternative allocation criteria extending beyond the size-and-number assigned within the MC are proposed. Until now there is no uniformity concerning the most valid alternative criteria. It is a fact however, that an increased percentage of patients with HCC undergoes transplantation beyond conventional indications. Recently, the use of (non-specified) expanded criteria has also been cited in international guidelines which leads to non-uniformed allocation protocols. Therefore further validation of these new expanded criteria is an urgent need.

Aim: This retrospective, multicentric study has the objective to investigate the value of the up-to-7 criteria (with seven being the maximal allowed sum of the size of the largest tumor (in cm) and the number of tumors for any given HCC) compared to the MC as gold standard. For this purpose we evaluated if there was a difference in survival and risk of recurrence between patients within MC compared to patients beyond the MC, but within the up-to-7 criteria.

Methods: We analyzed 378 patients transplanted for non-metastatic HCC from 5 different transplant centers in Belgium (Ghent University Hospital, University Hospitals of Leuven, Erasme Hospital Free University of Brussels, University Hospital of Liège, University Hospital of Antwerp) between 1999 and 2015. Patient groups were determined according to radiological MC and up-to-7 criteria at listing. We did not consider microvascular invasion (MVI) for the up-to-7 criteria because this parameter is not available at listing in routine clinical practice. To validate this method we compared the survival and recurrence between patients within the up-to-7 criteria in the presence or absence of MVI. We also assessed the correct estimation rate of pre-operative radiological staging compared to post-operative histological staging.

Results: In our cohort analysis based on pathological examination showed that 36,5% of patients were beyond MC and 25,1% beyond the up-to-7 criteria . Assessment of the accuracy of pre-operative radiological staging at listing resulted in a total discrepancy of 29,4% (22,0% understaged, 7,4% overstaged) for the MC and 20.1% (17,2% understaged, 2,9% overstaged) for the up-to-7 criteria. There was a statistical significant difference between the group of patients within MC compared to patients beyond MC in 5-year overall survival (75,1% vs. 53,2%, p=0.001) and recurrence rate (10,9% vs. 30,0%, p=<0,0001). With similar results for the up-to-7 criteria (73.7% vs. 43.1%, p=<0.001 and 11,9% vs. 43,0%, p=<0,0001 respectively). We found no significant difference in 5-year overall survival rate between the subgroup of patients within MC vs. patients beyond MC but within the up-to-7-criteria (75,1% vs. 63,8%, p= 0,259). However the latter subgroup had a tendency towards higher recurrence rate (10,9% vs. 19,0%, p=0,105). Adjusting the up-to-7 criteria according to the presence of microvascular invasion on explant pathology resulted in a worse outcome. The 5-year overall survival and recurrence rate was 67,3% and 14,9% in the absence of microvascular invasion compared to 47,9% and 22,2% respectively in the subgroup of patients with microvascular invasion.